

## **REMARKS**

Claims 14, 17, 24, and 30-33 have been amended; the amendments find support in the specification (for example, at page 14, lines 5-7) and in the claims as filed; no new matter has been added.

### **Restriction and Election**

Applicant acknowledges the withdrawal of claims 22 and 29 in response to the Examiner's request; however, a clarification is requested regarding the status of these claims, as to whether the Examiner considers them to represent a separate group (and thus a separately patentable invention), or a distinct species from the claims being currently considered. Pending such clarification, these claims have been withdrawn but not canceled.

### **Priority**

SEQ ID NO:5 (amino acids 22 through 227 of SEQ ID NO:2) *is* entitled to the benefit of the filing date of the 60/113,820 priority application – **December 23, 1998** – for the reasons set forth below.

The Office Action incorrectly states at page 2 that the provisional application "fails to provide the sequence of SEQ ID NO:5 therefore the priority date December 22, 1999 would be considered for the priority date, which is the filing date of [the later filed] PCT/US99/30523 application". This assessment does not take into account the fact that SEQ ID NO:5 *is identical to* amino acids 22 through 227 of SEQ ID NO:2, and *was* disclosed as amino acids 22 through 227 of SEQ ID NO:2 in the 60/113,820 priority application, filed **December 23, 1998**. The 60/113,820 priority application disclosed SEQ ID NO:2 at pages 9-10 of the 60/113,820 specification, and contains the following text (pages 12-13): "A preferred nucleotide sequence of the invention is SEQ ID NO:1, as set forth above, particularly nucleotides 79-1200 which encode the predicted full length translation product (amino acids 1-374 of SEQ ID NO:2). ... Nucleotides 142 to 759 encode the predicted extracellular coding domain (amino acids 22 to 227), with nucleotides 148 to 759 (amino acids 24 to 227) and 151 to 759 (amino acids 25 to 227) as possible alternatives." Therefore, amino acids 22 through 227 of SEQ ID NO:2 were disclosed as a distinct portion of SEQ ID NO:2 in the 60/113,820 application, with a priority date of December 23, 1998. In the PCT/US99/30523 application, the designation "SEQ ID NO:5" was applied to amino acids 22

through 227 of SEQ ID NO:2 in order to facilitate the preparation of a Sequence Listing to be filed with the PCT/US99/30523 application.

As described above, the sequence of SEQ ID NO:5 is identical to amino acids 22 through 227 of SEQ ID NO:2, and thus the term "SEQ ID NO:5" is synonymous with the term "amino acids 22 through 227 of SEQ ID NO:2". In order to simplify the claims, they have been amended to refer only to "amino acids 22 through 227 of SEQ ID NO:2" instead of to "SEQ ID NO:5"; this amendment is not a narrowing amendment because (in claims 14, 24, 30, and 31) one synonymous term is used instead of two synonymous terms or (in claims 17, 32, and 33) one synonymous term is substituted for another.

Given the support for the amino acid sequence of amino acids 22 through 227 of SEQ ID NO:2 in the priority application, and thus for SEQ ID NO:5 which is identical to amino acids 22 through 227 of SEQ ID NO:2, SEQ ID NO:5 (amino acids 22 through 227 of SEQ ID NO:2) *is* entitled to the benefit of the **December 23, 1998** filing date of the 60/113,820 priority application.

Rejection under 35 U.S.C. § 112, First Paragraph

Claims 14-21, 23, 24-28, and 30-33 were rejected under 35 U.S.C. § 112, first paragraph as purportedly lacking enablement. For the reasons provided below, this rejection is respectfully traversed.

The Office Action refers to **A)** methods of the invention providing certain soluble polypeptides (see claims 14 and 24), and also to **B)** methods of the invention providing certain soluble polypeptides that are at least 90% identical to amino acids 22 through 227 of SEQ ID NO:2 (also called SEQ ID NO:5), as recited in claim 30 and dependent claims 31-33. These methods of the invention will be addressed in turn below.

**A. Methods of the invention providing certain soluble polypeptides.** Claim 14 is drawn to a method involving an isolated soluble polypeptide comprising an amino acid sequence from the extracellular domain of the ss3939 polypeptide, the amino acid sequence being selected from the group consisting of amino acids 22 through 227 of SEQ ID NO:2, amino acids 24 through 227 of SEQ ID NO:2, and amino acids 25 through 227 of SEQ ID NO:2. Claim 24 is similar to claim 14, but recites an amino acid sequence from the extracellular domain of the ss3939 polypeptide comprising amino acids 22 through 227 of SEQ ID NO:2. Therefore, it is to be noted that the methods of claims 14 and 24 and their dependent claims involve soluble polypeptides that comprise certain specified amino acid

sequences of SEQ ID NO:2, these sequences being portions of the extracellular domain of the ss3939 polypeptide.

In addition, the specification teaches several approaches to making such soluble polypeptides. The Office Action notes only a part of this disclosure, i.e. that the specification teaches a "specifically referenced Fc fusion protein, such as ss3939/Fc referenced in Examples 2 and 5". However, the specification also describes (at the bottom of page 14 through the top of page 15) general methods for making soluble ss3939 polypeptides and, beginning at the bottom half of page 19 and running through the top of page 24, the specification teaches methods for making oligomeric forms of soluble ss3939 polypeptides, including the use of Fc polypeptides and leucine zipper polypeptides.

Further, the specification refers (at page 1) to knowledge in the art regarding the carbohydrate-binding properties of C-type lectin domains, and states at the top of page 11 that the ss3939 extracellular domain is similar to C-type lectin domains, such as those of macrophage mannose receptor. Therefore, given that the soluble ss3939 polypeptides of claims 14 and 24 and their dependent claims comprise the ss3939 extracellular domain (e.g. amino acids 22 through 227, or 24 through 227, or 25 through 227 of SEQ ID NO:2; see the bottom of page 10 of the specification), the soluble ss3939 polypeptides of claims 14 and 24 have C-type lectin (carbohydrate-binding domain) residues as does the ss3939/Fc polypeptide described *inter alia* in Examples 2 and 5 of the specification, and are expected to have the same property of binding to human umbilical vein endothelial cells.

Therefore, the specification provides sufficient description to enable those of skill in the art to make and use soluble ss3939 polypeptides of the invention as recited in claims 14 and 24 and their dependent claims; withdrawal of the rejection of these claims under 35 U.S.C. § 112, first paragraph, is respectfully requested.

**B. Methods of the invention providing soluble polypeptides that are at least 90% identical to amino acids 22 through 227 of SEQ ID NO:2.**

In assessing the enablement of claim 30 and its dependent claims 31-33, the Office Action discusses a few of the *In re Wands* factors (at pages 4-5 of the Office Action), but the Office Action does not address at all the factors that are the most important aspect in assessing enablement: the state of the prior art and the relative level of skill of those skilled in the art. It would be advantageous to consider these factors first, before any of the other *Wands* factors, because the sufficiency of a disclosure to enable certain claims must always be

assessed in light of what is *sufficient to enable those of skill in the art* to practice the claimed invention.

In order to provide some examples of the knowledge in the prior art and the level of skill of those in the art regarding C-type lectins and their structures and properties, Exhibits 1 and 2 are provided herewith. Exhibit 1 (Bajorath, J., 1996, "A molecular model of the carbohydrate recognition domain of a rat macrophage lectin and analysis of its binding site", *Journal of Molecular Graphics* 14: 297-301) states, for example in the right-hand column on page 297 of Exhibit 1, that the crystal structures of two C-type lectin proteins — mannose-binding protein (or "MBP") and E-selectin protein — had been determined by 1996, and that an analysis of mutant forms of MBP had determined the structures related to carbohydrate (mannose or galactose) specificity of MBP. Based on this knowledge in the art of the relationship between the primary amino acid sequences of MBP and E-selection, their three-dimensional structures, and their carbohydrate-binding function, Bajorath in Exhibit 1 uses the sequence alignment and structural modeling tools available to those of skill in the art to indicate the residues in a macrophage lectin (ML) protein that are involved in carbohydrate binding (see Figure 1 of Exhibit 1). Therefore, those of skill in the art such as the author of Exhibit 1, at the time of the filing of the 60/113,820 priority application (December 23, 1998), were clearly capable of discerning the residues of ss3939 polypeptide (SEQ ID NO:2) that are involved in the binding activity of ss3939 polypeptide. An example of such an analysis is shown in Exhibit 2, in which the amino acid sequence of ss3939 (SEQ ID NO:2) is aligned with the amino acid sequences of MBP and E-selection, and with the ML amino acid sequence described in Exhibit 1. Exhibits 1 and 2 demonstrate that those of skill in the art would readily be able to determine which residues in the extracellular C-type lectin domain of ss3939 polypeptide are in positions corresponding to structurally conserved regions of MBP and E-selection.

Given the knowledge in the art and the level of skill in the art as described above, it would be routine for those of skill in the art to determine which residues in SEQ ID NO:2 were critical for function, and to make variants of the amino acid sequence of amino acids 22 through 227 of SEQ ID NO:2 with changes in non-conserved regions, for example, that would be expected to retain activity such as the ability to bind to human umbilical vein endothelial cells. Making and testing such variants for activity as described in Examples 2 and 5 of the specification is routine and well within the skill of those in the art. When viewed in the context of the ability of those of skill in the art to model the structure of any proposed variant and to compare it to the known three-dimensional structures and carbohydrate binding

sites of C-type lectins such as MBP and E-selectin, it would not require undue experimentation to make variants that are at least 90% identical to amino acids 22 through 227 of SEQ ID NO:2 and that bind to human umbilical vein endothelial cells.

For at least the above reasons, withdrawal of the rejection of claims 14-21, 23, 24-28, and 30-33 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 16, 26, and 30-33 were rejected under 35 U.S.C. § 112, second paragraph, for an alleged lack of clarity. For the reasons presented below, this rejection is respectfully traversed.

The Office Action states that claims 16 and 26 are indefinite because of the use of the phrase "one or more". The meaning of this phrase appears to be clear as meaning the same thing as the expression "at least one". Thus, claims 16 and 26 are directed to embodiments where the binding partner of the ss3939 polypeptide comprises at least one polysaccharide moiety. The Examiner is respectfully requested to explain with particularity why this phrase is unclear, and in the absence of such grounds for rejection, it is respectfully requested that this rejection of claims 16 and 26 be withdrawn.

The Office Action states that claims 30-31 and 32-33 are indefinite as to the "biological activity, sequence and physical characteristics of the fragments" in the case of claims 30-31, and as to the "biological activity, size, sequence and physical characteristics of the mutants" in the case of claims 32-33. It is not clear what 'fragments' or 'mutants' the Office Action is referring to in these claims, but assuming *arguendo* that it is the soluble polypeptide of claim 30 that is at issue, it is respectfully pointed out that the last line of claim 30 recites that the soluble polypeptide has the biological activity of binding to human umbilical vein endothelial cells. Further, the soluble polypeptide has an amino acid sequence that is 90% identical to that of amino acids 22 through 227 of SEQ ID NO:2, which characterizes the soluble polypeptide in terms of sequence. Claim 30 as amended refers to a soluble polypeptide that comprises at least 20 contiguous amino acids of SEQ ID NO:2, providing further characterization of the size of the soluble polypeptide. Finally, it is not clear what other 'physical characteristics' of the 'fragments' or 'mutants' the Office Action is referring to. Therefore, claims 30-31 and 32-33 recite characteristics of the soluble polypeptide of the claims, and the Examiner is respectfully requested to explain further and with particularity why these claims are unclear, and in the absence of such grounds for



rejection, it is respectfully requested that this rejection of claims 30-31 and 32-33 be withdrawn.

The Office Action states that claims 32 and 33 are indefinite "because it is not clear how many amino acid residues are deleted, inserted or substituted in relation to the sequence of SEQ ID NO:5". Claims 32 and 33 recite that the soluble polypeptide has *from one to ten* deletions, insertions, or substitutions (in the case of claim 32) or substitutions (in the case of claim 33). The Examiner is respectfully requested to explain with particularity why the phrase "from one to ten" is unclear, and in the absence of such grounds for rejection, it is respectfully requested that this rejection of claims 32 and 33 be withdrawn.

For at least the above reasons, withdrawal of the rejection of claims 16, 26, and 30-33 under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Rejection under 35 U.S.C. § 102(a)

Claims 16, 20, 26, 28, 30, 31, and 32 were rejected under 35 U.S.C. § 102(a) as anticipated by Wood *et al.* (WO 99/14328; March 25, 1999). For the reasons presented below, this rejection is respectfully traversed.


For the reasons described in this paper in reference to SEQ ID NO:5, identical to amino acids 22 through 227 of SEQ ID NO:2 which is disclosed in the 60/113,820 priority application with a filing date of December 23, 1998, **the claims are entitled to the priority date of December 23, 1998.** Therefore, the Wood *et al.* reference (WO 99/14328, with a publication date of March 25, 1999) cannot properly be considered a prior reference under 35 U.S.C. § 102(a) with respect to the claims. For this reason alone, the rejection should properly be withdrawn.

In addition, the claims as presented all recite methods for inhibiting binding between an ss3939 polypeptide and a binding partner of said ss3939 polypeptide, *wherein the binding partner of said ss3939 polypeptide is expressed by human umbilical vein endothelial cells.* The Office Action does not point to any teaching in the Wood *et al.* reference of a binding partner of the ss3939 polypeptide expressed in human umbilical vein endothelial cells, and so the Office Action does not provide adequate grounds for the anticipation of the claimed methods by the Wood *et al.* reference.

For at least the above reasons, withdrawal of the rejection of claims 16, 20, 26, 28, 30, 31, and 32 under 35 U.S.C. § 102(a) is respectfully requested.

If a telephone interview would be helpful in advancing the prosecution of this application, Applicants' attorney invites the Examiner to contact her at the number provided below.

Respectfully submitted,



Suzanne A. Sprunger, Ph.D.  
Attorney for Applicants  
Registration No. 41,323  
Telephone (206) 265-7071

Amgen Inc.  
Law Department  
1201 Amgen Court West  
Seattle, WA 98119